2009

Breast Cancer Screening in Women Exposed In Utero to Diethylstilbestrol

Elizabeth A. Camp
University of Texas Health Science Center at Houston

Ann L. Coker
University of Kentucky, ann.coker@uky.edu

Stanley J. Robboy
Duke University, Stanley.Robboy@duke.edu

Kenneth L. Noller
University of Massachusetts Medical School Worcester

Karen J. Goodman
University of Texas Health Science Center at Houston

See next page for additional authors

JOURNAL OF WOMEN'S HEALTH
Volume 18, Number 4, 2009

DOI: 10.1089/jwh.2007.0580

Breast Cancer Screening in Women Exposed *In Utero* to Diethylstilbestrol

Elizabeth A. Camp, MSPH,[1] Ann L. Coker, Ph.D.,[1] Stanley J. Robboy, M.D.,[2] Kenneth L. Noller, M.D.,[3] Karen J. Goodman, Ph.D.,[1] Linda T. Titus-Ernstoff, Ph.D.,[4] Elizabeth E. Hatch, Ph.D.,[5] Arthur L. Herbst, M.D.,[6] Rebecca Troisi, Sc.D.,[7] Raymond H. Kaufman, M.D.,[8,9] and Ervin Adam, M.D.[8,10]

Abstract

Purpose: To determine if women exposed *in utero* to diethylstilbestrol (DES) are more likely than unexposed women to receive recommended or additional breast cancer screening examinations.
Methods: 1994 Diethylstilbestrol-Adenosis (DESAD) cohort data are used to assess the degree of recommended compliance of breast cancer screenings found in 3140 DES-exposed and 826 unexposed women. Participants were enrolled at four sites: Houston, Boston, Rochester, and Los Angeles. Logistic regression modeling was used to analyze mailed questionnaire data that included reported frequency over the preceding 5 years (1990–1994) of breast-self examinations (BSEs), clinical breast examinations (CBEs), and mammograms.
Results: DES-exposed women exceeded annual recommendations for CBEs (aOR 2.20, 95% CI, 1.04-4.67) among women without a history of benign breast disease (BBD) compared with unexposed women. There were no other statistically significant differences between exposed and unexposed women who reported performing BSEs, CBEs (<40 years of age), and mammographies, regardless of BBD history.
Conclusions: The majority of DES-exposed women receive breast cancer screenings at least at recommended intervals, but over two thirds do not perform monthly BSEs. Future efforts should be focused on further educating this and other at-risk populations through mailed reminders and during patient consultations on the benefits of screening examinations.

Introduction

Diethylstilbestrol (DES), a nonsteroidal estrogen first synthesized in 1938, was given to women to prevent miscarriages by increasing their progesterone hormone levels.[1,2] In 1971, it was found to cause a rare vaginal adenocarcinoma, seen in young women born in the New England area.[3] That same year, the Federal Drug Administration (FDA) halted its use during pregnancy.[4] Subsequently, the Diethylstilbestrol-Adenosis (DESAD) project was formed to examine the scope of the public health issue and to help provide recommendations. It has been estimated that a total of 267 pharmaceuticals companies manufactured DES in the United States during the period of its use, and estimates of the number of white, middle-class women prescribed DES while pregnant during the years 1957–1971 (the peak years of use) are in the range of 2–10 million.[2,5] The project originally comprised four centers: Baylor College of Medicine, Houston, Texas; Massachusetts General Hospital, Boston, Massachusetts; the Mayo Clinic, Rochester, Minnesota; and the University of Southern California, Los Angeles, California.[6] The purpose of this DESAD project was to follow the exposed population

[1]School of Public Health, University of Texas Health Science Center, Houston, Texas.
[2]Departments of Pathology and Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina.
[3]Department of Obstetrics and Gynecology, University of Massachusetts Medical Center, Worcester, Massachusetts.
[4]Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.
[5]Department of Epidemiology and Biostatistics, Boston University School of Public Health, Boston, Massachusetts.
[6]Department of Obstetrics and Gynecology, University of Chicago, Chicago, Illinois.
[7]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland.
[8]Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, Texas.
[9]Department of Obstetrics and Gynecology, Methodist Hospital, Houston, Texas.
[10]Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas.

through a prospective study.[6] The councils of the American College of Obstetrics and Gynecologists (ACOG), along with the National Institutes of Health (NIH), recommended continued follow-up of this *in utero*-exposed group.[7]

Several studies have examined the risk of breast cancer in women who were either exposed *in utero* to DES or prescribed the drug while pregnant.[8–13] In a 2002 study by Palmer et al;[8] DES-exposed daughters >age 40 were found to have a 2.5 fold increased risk for breast cancer. Similarly, in a later study, DES-exposed women >age 40 were discovered to have an almost 2-fold increased risk for breast cancer, and women >age 50 were estimated to have a 3-fold increased risk.[13] A slight risk for breast cancer in mothers who ingested DES orally has been seen in other studies.[9–12] In light of this possible increased risk, this current study examines whether women exposed *in utero* to DES are more likely to receive recommended or additional breast cancer screening examinations compared with unexposed women.

Materials and Methods

Patient recruitment, including follow-up information for this cohort has been described.[3,4,14] Briefly, DES-exposed women were recruited through information gathered through record review, physician referral, or walk-ins through four main centers located throughout the United Sates. These locations included rural as well as urban populations located at the center sites, Boston, Rochester, Houston, and Los Angeles. The unexposed women were recruited from information available in prenatal medical records during that time. Siblings of the exposed women, along with women recruited through record review, were matched on exposed women's age within 6 months and on her mother's age during pregnancy within 5 years. At the start of 1975 through 1983, both exposed and unexposed participants were examined annually. They were then followed with a yearly questionnaire from 1984 to 1989.[6,15] Again in 1994, self-administered questionnaires were mailed to previous DESAD participants.[15] This study has been reviewed and approved by Institutional Review Boards at each participating study site.

Recommendation definitions

Information describing breast cancer screening behaviors was obtained from the 1994 questionnaire, which included the number of clinical breast examinations (CBEs) and mammograms and the frequency of breast self-examinations (BSEs). The time period of the self-reported screening behavior was between 1990 and 1994. Because the data were not verified through chart review, the results are the women's perceptions of their behavior. Screening is divided by a previous diagnosis of benign breast disease (BBD) to determine if any behavior differences exist between the two populations with a previous breast diagnosis. Frequency was divided into a compliant group and exceeded recommendation group to further study the behavior differences of the exposed and unexposed populations.

During the study period, there were no specific breast cancer screening recommendations for *in utero* DES-exposed women.[16,17] Therefore, the recommendations for the unexposed population were applied to all women in this study. In the 5 years prior to 1994, the Council on Scientific Affairs along with the American Cancer Society recommended a monthly BSE for all women >age 20 and a CBE every 3 years in women aged 20–39 and annually for women aged ≥40. Furthermore it was suggested that women aged 40–49 receive a mammogram every 1 or 2 years and annually for women >age 50.[18,19]

Compliance for BSE was defined for all age groups as occurring once a month or more, and noncompliance was defined as every 2–3 months or less often. For CBE, compliance for women aged 20–39 was defined as once in the past 5 years, and exceeding recommendations was defined as two to three times or more, with none in the past 5 years as the reference group. Additionally, compliance for CBEs in women aged 40–49 was defined as four or five CBEs, and exceeding recommendations was defined as more than five CBEs in the same time frame. Both of these groups were compared with women reporting fewer than four CBEs. Similarly, for mammography, compliance for women aged 40–49 was defined as having had a mammogram two or three times in the past 5 years, and exceeding recommendations was defined as four or more mammograms. After 5 years was subtracted from the women's ages at the time of the survey (to place women in their appropriate recommendation by age for mammography and CBEs), no exposed or unexposed women in the study group were >age 49.

Data analysis

The analysis addressed the association between DES exposure and reported frequency of breast cancer screenings. Analysis showing patterns of breast cancer screening (BSEs, mammography, and CBEs) in relation to DES exposure was evaluated by strata of BBD, as a slightly increased risk for breast cancer had been found in DES-exposed mothers.[9–12] A family history of any cancer was also analyzed to determine any difference between the two groups. All statistical evaluation was performed using SPSS 11.0 statistical software (SPSS, Inc., Chicago, IL.) and EpiInfo 6.04d (Geneva, Switzerland).

Although the parent study used a prospective cohort design, adjusted odds ratios (aOR) were chosen as the relevant measure of association between DES exposure status and screening frequency in the past 5 years to control for multiple variables through logistic regression. Three of the four dependent outcome variables had three frequency levels (BSEs had only two levels). Separate binary (i.e., compliant vs. noncompliant and exceeding recommendations vs. noncompliant) logistic regression models were used to estimate the ORs and 95% confidence intervals (CI) for each of the two outcome categories that met or exceeded recommendations compared with the reference category.[20]

Potential confounders for exposure-outcome associations assessed in this study included age (in 5-year categories), marital status (single, married, or widowed/divorced/separated), education (high school and post-high school, junior college, full college, and graduate school), and study site. All these were included in the final models, as their inclusion resulted in a 10% or greater change between the crude and adjusted estimates for the exposure-outcome association when comparing the crude and adjusted associations.[21] Furthermore, these potential confounders may directly influence the decision of the women in regard to compliance. The Breslow-Day test for homogeneity was used to determine if the association between DES exposure and screening behaviors

differed by BBD and a family history of cancer. A two-sided p value of ≤ 0.25 was considered evidence of effect measure-modification.[20]

The Yates two-sided p value was used to test differences in the screening frequency between exposed and unexposed women. Unconditional logistic regression was used to estimate the adjusted prevalence ORs for DES-exposed women categorized by their screening frequency levels. The ordinal variable that described their screening frequency was included in the logistic regression models to assess whether DES exposure was associated with a trend toward increased screening frequency. To describe this trend, the Wald two-sided p value test was presented.[22]

Results

Descriptive findings

Response rates for the 1994 questionnaire were high for all centers: 96% of the exposed and 98% of the unexposed women at the Boston Center, 96% of both exposed and unexposed women at the Rochester Center, 84% of the exposed and 91% of the unexposed at the California Center, and 89% of the exposed and 83% of the unexposed women at the Houston Center.

The total number of study participants who responded to the 1994 questionnaire included 3140 exposed women and 826 unexposed women, 98% of whom were Caucasian. The remainding 2% consisted of blacks, Hispanics, Asian or Pacific islanders, and others. Among the exposed women who responded to the 1994 questionnaire, 46% were originally recruited into the cohort through record review, 33% were recruited through physician referral, and 21% were walk-ins. In the unexposed population, 75% were recruited through record review, and 25% were siblings of exposed women.

Multivariate analysis

DES-exposed women were similar to unexposed women on study variables with the following exceptions (Table 1): unexposed women were older (unexposed mean age = 42, and DES-exposed mean age = 40; Yates two-sided $p < 0.0001$), and DES-exposed women were more highly educated ($p < 0.0001$) than unexposed women (those whose education did not exceed high school, including nongraduates, and those with post-high school vocational training were compared with those with the higher levels of junior college through graduate school). There was no significant difference between exposed and unexposed women regarding marital status ($p = 0.98$); however, a difference was detected between urban and rural locations (Boston, California, and Houston were combined and compared with Mayo) ($p = 0.02$). Furthermore, the chi-square and Yates two-sided p value for BBD and family history of cancer were found to be nonsignificant (chi-square = 0.01, $p = 0.936$; chi-square = 0.47, $p = 0.495$, respectively). The Breslow-Day test for homogeneity resulted in a p value of 0.116 for compliant BSEs and DES exposure. There was no effect modification found for family history of cancer.

DES-exposed and unexposed women had similar frequencies of BSEs in the past 5 years [aOR (adjusted OR) 1.04, 95% CI (confidence interval) 0.87-1.25] (data not shown). This finding held if there was a history of BBD (aOR 1.29, 95% CI 0.92-1.82) or no such history (aOR 0.96, 95% CI 0.78-1.19).

Table 1. Demographic Characteristics and Benign Breast Disease History in DES-Exposed and Unexposed Women

	DES exposed (n = *3,140*)		*DES unexposed* (n = *826*)	
Characteristic	n	%	n	%
Age, years				
25–29	50	2	0	0
30–34	354	11	30	4
35–39	877	28	263	32
40–44	1296	41	301	36
45–49	533	17	200	24
50–55	30	1	32	4
Education				
Less than high school and post-high school	402	13	152	18
Junior college	724	23	197	24
4-year college	1125	36	257	31
Graduate school	880	28	217	26
Missing	9	0.3	3	0.4
Marital status				
Single	410	13	113	14
Married	2261	72	591	72
Widowed/divorced/ separated	425	14	105	13
Missing	44	1	17	2
Site				
Boston	921	29	321	39
Rochester	588	19	186	23
Los Angeles	803	26	172	21
Houston	828	26	147	18
History of benign breast disease				
Yes	777	25	207	25
No	2350	75	619	75
Missing	13	0.4	0	0
History of family cancer[a]				
Yes	1265	40	344	42
No	1831	58	470	57
Missing	44	1	12	2

[a]The term family encompasses parents, siblings, and children.

Among both exposed and unexposed women, the proportion of women performing monthly BSEs (27% and 26%, respectively) and BSEs every 2–3 months (30% and 29%, respectively) was very low.

DES-exposed women <age 40 had similar reported frequencies of CBE compared with unexposed women (aOR 1.17, 95% CI 0.59-2.32) (data not shown). This finding held whether the women were defined as compliant or exceeding recommendations, or whether or not they had a previous history of BBD. When the adjusted analysis was further stratified on a history of BBD, the aOR was 2.04; however, the CI was extremely wide (95% CI 0.24-17.38, $n = 11$). There was no difference found between the two exposure groups in the unadjusted OR analysis.

When restricting the analysis to women who were at greater risk of breast cancer based solely on age (40–49), DES-exposed women relative to the unexposed women were moderately more likely to report more than five CBEs in the past 5 years (aOR 1.67, 95% CI 0.95-2.96) (Table 2). Among women without BBD, however, those who were DES-exposed appeared to have more than five CBEs in the past 5 years (aOR 2.20, 95% CI

Table 2. Adjusted Odds Ratios and 95% Confidence Intervals for Clinical Breast Examinations (CBEs) in Past 5 Years (1990–1994) in DES-Exposed and Unexposed Women Aged 40–49

	DES exposed (n = 563)		*DES unexposed* (n = 232)				
	n	%	n	%	*Adjusted OR*[a,b]	*95% CI*[a]	p *for trend*[c]
Number of CBEs in past 5 years[d]							
Missing[e]	4	0.7	2	0.9			
None	18	3	8	3			
Once	46	8	22	10			
2–3 times[f]	149	27	60	26	1.00	Referent	
4–5 times[g]	255	45	116	50	0.97	0.68–1.37	
>5 times[h]	91	16	24	10	1.67	0.95–2.96	0.39
Reported history of BBD[a] (n = 252)							
	DES exposed (n = 173)		*DES unexposed* (n = 79)				
	n	%	n	%	*Adjusted OR*[a,b]	*95% CI*[a]	p *for trend*[c]
Number of CBEs in past 5 years[d]							
None	1	0.6	2	3			
Once	11	6	6	8			
2–3 times[f]	37	21	15	19	1.00	Referent	
4–5 times[g]	86	50	45	57	0.87	0.44–1.70	
>5 times[h]	38	22	11	14	0.83	0.29–2.35	0.52
Reported No history of BBD[a] (n = 533)							
	DES exposed (n = 382)		*DES unexposed* (n = 151)				
	n	%	n	%	*Adjusted OR*[a,b]	*95% CI*[a]	p *for trend*[c]
Number of CBEs in past 5 years[d]							
None	17	5	6	4			
Once	35	9	16	11			
2–3 times[f]	110	29	45	30	1.00	Referent	
4–5 times[g]	168	44	71	47	1.08	0.70–1.65	
>5 times[h]	52	14	13	9	2.20	1.04–4.67	0.36

[a]OR, odds ratio; CI, confidence interval; BBD, benign breast disease.
[b]Adjusted for age (continuous variable), education, marital status, and site.
[c]The *p* value (two-sided) for trend included all five outcome frequency categories; none of the frequency categories were combined for the trend test.
[d]Five years [(1994–birth year) − 5] were subtracted from the current questionnaire age to put the women's respective screening age in the proper context of the previous 5 years: no women >age 50 were present in the dataset, and only 20% were aged 40–49.
[e]Missing values indicate a nonresponse to the question regarding number of CBEs in the past 5 years.
[f]Categories (none, once, and 2–3 times) were combined to form the reference category.
[g]The category 4–5 times was compared to the reference group and defined as compliant for CBE screening for this age group.
[h]The category >5 times was compared to the reference group and defined as exceeding recommendations for CBE screening for this age group.

1.04-4.67) compared with DES-unexposed women, although DES exposure was not associated with a trend toward increasing CBE frequency (*p* value for trend = 0.36).

DES-exposed and unexposed women aged 40–49 were similar in compliance (two or three times in the past 5 years) with mammography screening (45% vs. 44%) (aOR 1.03, 95% CI 0.68-1.55) (data not shown). A similar pattern of compliance was found in women with and without a history of BBD. Among women who reported a history of BBD, 41% were compliant compared with 36% of the unexposed (aOR 1.53, 95% CI 0.65-3.60). Of the women who reported no history of BBD, 48% of the exposed women were compliant compared with 49% in the unexposed group (aOR 1.00, 95% CI 0.62-1.63).

The analysis was repeated, but this time the women who never had a screening examination within the past 5 years were removed from the noncompliant group. The second analysis was performed to test the assumption that these women may be fundamentally different from those who have had at least one screening examination. The results from the secondary analysis were no different from the first; therefore, it can be concluded that there is no statistical difference between the semicompliant behavior (at least one screening examination in the past 5 years) and the noncompliant behavior (no screening examinations in the past 5 years).

Discussion

The results of this study showed that DES-exposed women (aged 40–49) were not consistently more likely than unexposed women to be in compliance with recommended

screening for BSE or for mammography screening. Among women without a history of BBD, however, DES-exposed women report more CBEs (done by a healthcare provider) than do unexposed women. A possible explanation for this finding may involve compliance with the women's health examination, where in addition to cervical screening, breast cancer screening is performed by a clinician. Recently, DES-exposed women were found to be overly compliant when it came to Pap smear examinations and general physical examinations, which could explain the overcompliance for CBEs in this study.[23] The compliance for CBEs could be driven by cervical cancer screening rather than breast cancer screening.

It has been estimated that for the years 1987–1992, 48.3% of women reported receiving a CBE, but only 38.2% were found through chart review, and 49.0% of women reported having a mammogram, but only 42.4% were verified in medical records.[24] In comparison with this analysis group aged 40–49, 45% of the DES-exposed group and 50% of the unexposed reported being compliant with CBE recommendations. In the same age group, 45% of the exposed and 44% of the unexposed reported having a mammogram during the recommended time. The results found in our study are very similar to the results published in 1994.

A major strength of this study is that breast cancer screenings in the DES-exposed population have not been fully examined previously. A strength of the DESAD study was its efforts to address the problem of selection bias. To reduce selection bias that may result when study respondents disproportionately include volunteers compared with a more random population-based sample, medical records were linked with live birth data for exposed and unexposed women. Exposed women were then invited to participate in the study.[4] This strategy should have minimized selection bias, which can occur when more health-conscience volunteers participate in the study, resulting in an OR moving away from the null. Another strength of the DESAD study was its efforts to reduce loss to follow-up. All study sites had an interview response rate of at least 80% from the study inception, and some cohorts exceeded a 90% response rate, which is rare in any large study continuing over decades, especially when the controls are presumed normal and have no personal reason to continue in the study.

Study limitations included the potential for misclassification of the reported frequencies of cervical and breast cancer screenings and physical examinations. Although the DESAD study had an established diagnosis verification system, in the data used for this analysis, screening examinations and health conditions were not verified by pathologic study or medical reports. Therefore, this study relied solely on self-report of screening and prior health conditions that were examined as potential effect measure modifiers. This study may also have a possible selection bias in regard to screening frequency, as 25% of the unexposed were siblings of exposed women who may be more aware of cancer risk in general. This bias would result in an OR toward the null, although there was no significant difference between the exposed and unexposed groups in regard to family cancer history.

According to previous reports, women tend to over-report the frequency of breast cancer screening.[24,25] There is no evidence to suggest that DES-exposed women were more likely than unexposed women to overreport the frequency of screening examinations, although previous data showed that DES-exposed women were more likely than unexposed women to misreport their diagnoses.[7] If DES-exposed women overstated their screening frequency to a greater extent than unexposed women, the resulting OR would be biased away from the null value. If such a differential misclassification were the case, however, we would expect to observe positive associations for all screening examinations, but this did not occur. Further, for some of the examinations, the analysis shows similar screening frequencies among high-risk women regardless of DES exposure status, which is further evidence against a tendency for overreporting among exposed women.

Stratifying on a previous diagnosis of BBD led to small numbers for all screening examinations, which possibly weakened the power to detect a significant difference. There was a somewhat increased risk found for CBEs in women >age 40. The aim of the study was to determine compliance based on the women's perception of breast cancer risk. If the women had a previous diagnosis of BBD, their screening behavior might be influenced by this and, therefore, affect their number of breast cancer screening visits. Furthermore, as the self-reported questionnaire data do not report how participants were recruited, we were unable to remove siblings recruited through DES-exposed daughters, whose sisters' cancer experience may affect their own screening behaviors. It is worth noting that there were few demographic differences between the exposed and unexposed women (Table 1).

The lack of insurance information in this study may cause confounding by healthcare access. If DES-exposed women were more likely than unexposed women to have insurance and, therefore, receive more frequent screening, insurance status, rather than DES exposure, would be the factor that led to more frequent screening. Potential confounding could only be operating if insurance status led to more frequent screening and was more common in DES-exposed women. We attempted to address this issue of potential confounding by adjusting for education and marital status, which are highly correlated with receiving preventive care[26,27] and being insured.[28]

Several papers with different conclusions discussed the importance of BSE as reviewed by Thomas et al.,[29] who did not find a reduction in mortality rates for breast cancer by BSE despite the intensive instruction given to participants in the procedure. No study, to our knowledge, has shown that excessive compliance to BSE (or any other breast prevention examination) increases detection for breast cancer; nevertheless, BSE remains a simple, cost-free procedure that may detect palpable abnormalities in the breast, leading to early professional consultation.

Conclusion

DES-exposed women were not different from unexposed women when reporting breast screening examinations, except when reporting receiving CBEs in women >age 39. Although the majority of women in the study were not yet of age for recommended mammography, these data suggest the DES-exposed women (73%) are keeping the recommendation for mammography screening and CBEs (61%), yet the majority failed to perform monthly BSE, with 73% not meeting the recommendation. The majority of this cohort today would be in their mid-50s to late 50s, putting them at increased risk for breast cancer.

Possible suggestions for improving all screening practices could include mailed reminders to schedule a wellness examination (when a CBE is typically performed) and a mammogram. Even though BSE have not been shown to reduce breast cancer mortality, patient consultation could include reminders to note any changes to the breast and to contact a provider if necessary. As this population ages, risks become higher, and prevention using the tools provided hopefully will improve detection or prevent advanced disease. Access to health insurance and access to general health information could be factors in lower compliance in preventive examinations. This DES-exposed population of women will require future efforts to notify them of their increased risk and remind them of the importance of preventive examinations.

Acknowledgments

This study was supported by the National Cancer Institute under contact 1-CP-21166.

Disclosure Statement

The authors have no conflicts of interest to report.

References

1. Tedeschi C. Ties that bind. Mothers, daughters and sons continue to feel effects of DES. Adv Nurse Pract 1999;7:28–34.
2. Laitman CJ. DES exposure and the aging women: Mothers and daughters. Curr Womens Health Rep 2002;2:390–393.
3. Herbst AL, Ulfelder H, Poskanzer DC. Adenocarcinoma of the vagina. Association of maternal stilbestrol therapy with tumor appearance in young women. N Engl J Med 1971;284: 878–881.
4. Federal Food and Drug Administration. Diethylstilbestrol contraindicated in pregnancy. FDA Drug Bull 1971.
5. Swan, SH. Intrauterine exposure to diethylstilbestrol: Long-term effects in humans. APMIS 2000;108:793–804.
6. Robboy SJ, Szyfelbein WM, Goellner JR, et al. Dysplasia and cytologic findings in 4,589 young women enrolled in the Diethylstilbestrol-Adenosis (DESAD) project. Am J Obstet Gynecol 1981;140:579–586.
7. ACOG Committee Opinion: Committee on Gynecologic Practice. Diethylstilbestrol. Int J Gynaecol Obstet 1994;44:184.
8. Palmer JR, Hatch EE, Rosenberg CL, et al. Risk of breast cancer in women exposed to diethylstilbestrol *in utero*: Preliminary results (United States). Cancer Causes Control 2002;13:753–758.
9. Colton T, Greenberg ER, Noller K, et al. Breast cancer in mothers prescribed diethylstilbestrol in pregnancy. Further follow-up. JAMA 1993;269:2096–2100.
10. Greenberg ER, Barnes AB, Resseguie L, et al. Breast cancer in mothers given diethylstilbestrol in pregnancy. N Engl J Med 1984;311:1393–1398.
11. Calle EE, Mervis CA, Thun MJ, Rodriguez C, Wingo PA, Health CW Jr. Diethylstilbestrol and risk of fatal breast cancer in a prospective cohort of U.S. women. Am J Epidemiol 1996;144:645–652.
12. Titus-Ernstoff L, Hatch EE, Hoover RN, et al. Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy. Br J Cancer 2001;84:126–133.
13. Palmer JR, Wise LA, Hatch EE, et al. Prenatal diethylstilbestrol exposure and risk of breast cancer. Cancer Epidemiol Biomarkers Prev 2006;15:1509–1514.
14. Hatch EE, Palmer JR, Titus-Ernstoff L, et al. Cancer risk in women exposed to diethylstilbestrol *in utero*. JAMA 1998; 280:630–634.
15. Kaufman RH, Adam E. Findings in female offspring of women exposed *in utero* to diethylstilbestrol. Obstet Gynecol 2002;99:197–200.
16. Bibbo M. Screening of individuals exposed to diethylstilbestrol. Clin Obstet Gynecol 1979;22:689–699.
17. Prenatal diethylstilbestrol (DES) exposure: Recommendations of the Diethylstilbestrol-Adenosis (DESAD) Project for the Identification and Management of Exposed Individuals. Bethesda, MD: National Cancer Institute, Office of Cancer Communications, Dept. DES, National Cancer Institute, 1980.
18. Council on Scientific Affairs. Mammographic screening in asymptomatic women aged 40 years and older. JAMA 1989; 261:2535–2542.
19. Shapiro S, Smart CR, Costanza ME, et al. Guidelines for breast cancer screening. Cancer 1992;69(Suppl 7):2001–2002.
20. Breslow NE, Day NE. Statistical methods in cancer research. Volume I. The analysis of case-control studies. IARC Scientific Publications, 1980:32:323–338.
21. Greenland S. Modeling and variable selection in epidemiologic analysis. Am J Public Health 1989;79:340–349.
22. Dwyer JH, Feinleib M, Lippert P, Hoffmeister H. Statistical models for longitudinal studies of health. New York: Oxford University Press, 1991:243–246.
23. Camp EA, Coker AL, Troisi R, et al. Cervical screening and general physical examination behaviors of women exposed *in utero* to diethylstilbestrol. J Low Genit Tract Dis 2008;12: 111–117.
24. Sudman S, Warnecke R, Johnson T, et al. Cognitive aspects of reporting cancer prevention examinations and tests. National Center for Health Statistics. Vital Health Stat 6(7). 1994.
25. Gordon NP, Hiatt RA, Lampert DI. Concordance of self-reported data and medical record audit for six cancer screening procedures. J Natl Cancer Inst 1993;85:566–570.
26. Huguley CM Jr, Brown RL, Greenberg RS, Clark WS. Breast self-examination and survival from breast cancer. Cancer 1988;62:1389–1396.
27. Brown AJ. Awareness and use of cervical cancer tests in a southern Appalachian community. Public Health Rep 1976;91:236–242.
28. Hagdrup NA, Simoes EJ, Brownson RC. Health care coverage: Traditional and preventive measures and associations with chronic disease risk factors. J Community Health 1997;22:387–399.
29. Thomas DB, Gao DL, Ray RM, et al. Randomized trial of breast self-examination in Shanghai: Final results. J Natl Cancer Inst 2002;94:1445–1457.

Address reprint requests to:
Raymond H. Kaufman, M.D.
6550 Fannin, Suite 900
Houston, TX 77030

E-mail: rkaufman@tmh.tmc.edu